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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/648,978	08/27/2003	Thomas Spies	FHCC:010US	4396

7590 06/09/2006

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EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/648,978	SPIES ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *4 and 14-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-25 are pending.

2. Applicant's election without traverse of Group II, claims 1-3 and 5-13 in the reply filed on 04/28/06 is acknowledged.

3. Claims 4 and 14-25 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 1-3 and 5-13 read on a method for expanding a human T-cell population that expresses a natural or engineered NKG2D comprising contacting said population with an NKG2D ligand,wherein said contact is performed *in vivo* are under consideration in the instant application.

5. Claims 1-3 and 5-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification only discloses *in vitro* assay , suggesting that: (i) NKG2D could enhance anti-CMV and presumably other cytotoxic CD8 αβ T-cell responses (see Example 2 in particular)

The specification does not adequately teach how to effectively expanding a human T-cell population that expresses a natural or engineered NKG2D by contacting said population with an NKG2D ligand, wherein said contact is performed *in vivo*. Moreover, no animals models were used to study the effectively of expanding a human T cells population that expresses a natural or engineered NKG2D by contacting said population with an NKG2D ligand. Since there is no animal model studies and data in the specification to show the effectively of expanding a human T-cell population that expresses a natural or engineered NKG2D by contacting said population with an NKG2D ligand, wherein said contact is performed *in vivo* it is unpredictable how to correlate *in vitro* results with *in vivo* use. The specification does not teach how to extrapolate data obtained from *in vitro* studies to the development of effective *in vivo* method for expanding a human T cell commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of the claimed method of expanding a human T-cell population that expresses a natural or engineered NKG2D by contacting said population with an NKG2D ligand, wherein said contact is performed *in vivo* The specification does not provide sufficient teaching and evidences as to how it can be assessed that effective *in vivo* expanding of human T cells population that expresses a natural or engineered NKG2D was achieved after contacting said population with any NKG2D ligand. Thus in the absence of working examples or detailed guidance in the specification, the intended uses of any NKG2D ligand in the claimed method for expanding a human T cell are fraught with uncertainties.

Jamieson et al., (Immunity, 2002, Vol.17, pages 19-29) teach that NKG2D cross-linking is not directly stimulatory in the case of preactivated mouse CD8+ T cells, which express abundant cell surface NKG2D. NKG2D signals differently in distinct immune cell types. (see entire document, page 26 in particular).

Maasho et al., (J of Immunology, 2005, V.174, pages 4480-4484) teach that NKG2D alone cannot stimulate naïve CD8+ T cells and only might act as a costimulatory receptor for TCR signaling (see entire document, page 4481 in particular).

Richie Ehrlich et al., (J of Immunology, 2005,V.174, pages 1922-1931) clearly stated that neither stimulation via mAB cross-linking nor NKG2D ligand engagement alone is sufficient to co-stimulate proliferation or effector function in primary mouse or human CD8+ T cell suggesting that NKG2D acts as a co-stimulatory molecule only under restricted conditions or requires additional cofactors. Richie Ehrlich et al., further teach that "we were unable to demonstrate a role for NKG2D in costimulating proliferation, cytolytic activity or IFN-γ production of naïve or effector splenic mouse CD8+ T cells or preactivated human peripheral blood CD8+ T cells. In all assays, CD28 costimulation was observed (see entire document, page 1929 in particular).

Cochlovius et al (Modern Drug Discovery, 2003, pages 33-38) teach that in contrast to in vitro models, and partly animal-human xenograft systems, tissue cells in vivo seems to express molecules for defense against cellular immune systems as well as against complement. Although these defense mechanisms are still poorly understood, they provide some hints as to why many potential therapeutics perform marvelously in vitro but a fairly high portion of them still fail in vivo.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed method for expanding a human T-cell population that expresses a natural or engineered NKG2D by contacting said population with an NKG2D ligand, wherein said contact is performed *in vivo* in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 571/273-8300

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MICHAIL BELYAVSKYI, PH.D.
PATENT EXAMINER
6/8/06